PREDICTION OF TUBULOINTERSTITIAL INJURY BY DOPPLER ULTRASOUND IN GLOMERULAR DISEASES : VALUE OF RESISTIVE AND ATROPHIC INDICES

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CERTIFICATE

This is to certify that **Dr. RAM PRABAHAR ,** is a bonafide student of Department of Nephrology , Madras Medical College and Government General Hospital, Chennai - 600 003 and his study on **" PREDICTION OF TUBULOINTERSTITIAL INJURY BY DOPPLER ULTRASOUND IN GLOMERULAR DISEASES : VALUE OF RESISTIVE AND ATROPHIC INDICES"** is a bonafide original work done by him, for his dissertation towards the partial fulfillment of the D.M NEPHROLOGY Degree. He has done this study under my supervision and guidance and no part of this study has been submitted for the award of any other degree or diploma.

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INTRODUCTION

Applications of Doppler Ultrasound in Nephrology are increasing day by day. Gray scale sonography is often routinely performed to evaluate the patient with suspected or known renal disease. Although this provides anatomic information it lacks the ability to provide significant physiologic data. Duplex Doppler ultrasound has the potential to provide physiologic information concerning renal arterial blood flow and resistance[1].

Studies published in the last two decades indicated that Doppler can be used reliably in several types of intrinsic renal diseases[2], obstructive uropathy[3], Acute renal failure [4] and Reno vascular hypertension[5].

Doppler has been found to be useful for detection of acute rejection[6] and also for distinction between obstructive and non obstructive pelvi calyceal system dilatation[3] .It is also widely used for diagnosis of Reno vascular hypertension with variable sensitivity and specificity[5]. In acute renal failure it is used to differentiate pre-renal azotemia from acute tubular necrosis and to predict recovery from acute tubular necrosis[4].

Apart from these, Doppler can be used to measure total and split renal function[7]. Increased RI atleast three months after transplantation is associated with poor subsequent allograft performance and death[8]. It has also been shown that resistive index may be useful as a non invasive marker to detect scarring in reflux nephropathy[9].

Among the Doppler derived indices, resistive index is the most studied parameter for quantifying the alterations in renal blood flow that may occur with glomerular diseases[15]. The diagnostic utility of Doppler in glomerular disease is under debate. Some studies show encouraging results[12, 20] whereas others are disappointing[13].

Although Doppler can't substitute renal biopsy studies have shown that it can be useful in prognostication and to quantitate the severity[14]. Tubulo interstitial lesions proven to be the best histologic correlate of long term renal survival in various glomerular diseases [18,21]. However this requires renal biopsy which is an invasive procedure.

This study was done to find out the utility of Doppler Ultrasound in glomerular diseases. Specifically the role of resistive and atrophic indices and the role of these indices as prognostic markers were evaluated.

AIMS AND OBJECTIVES

The objectives of the study are :

1. To find out the role of Doppler in glomerular diseases to predict extent of tubulointerstitial injury as demonstrated by renal biopsy.

2. The role of resistive and atrophic indices in predicting tubulointerstitial disease.

3. Value of these indices as prognostic markers to identify patients at risk of progression.

REVIEW OF LITERATURE

Ultrasonography is the most commonly used modality of imaging in Nephrology.[1] It is widely used because of its accessibility, low cost, non invasiveness, safety ,lack of ionizing radiation and contrast use. Although it has high accuracy to detect anatomical abnormalities, it provides little functional information.

Duplex Doppler ultrasound has the advantage of combining anatomic with functional information regarding renal arterial blood flow and resistance.[1] The presence or absence and the nature of blood flow details from Doppler improves its diagnostic utility. An appreciation of physical principles of Doppler effect is an essential pre requisite for interpretation of Doppler signals.

DOPPLER EFFECT

This is a phenomenon by which the frequency of sound wave received after reflection from moving target is shifted from that of the source. The change in frequency is called doppler shift. This occurs whenever the effective distance between the observer and source is changing with time.[23]

This phenomenon is observed in a variety of situations .By just listening to the sound which is changed in frequency ,a stationery listener can find out whether the object is receding or approaching. For this effect to appear it requires a source, receiver and medium. Medical ultrasound uses a stationary source and receiver, and it is the properties of the medium that produces this effect.

Christian Andreas Doppler[23] enunciated his principle in 1842 . However he confused its interpretation to explain the color of binary stars. Acoustical Doppler effect was demonstrated by Buys Ballot in 1845. He used a trumpeter riding on a steam locomotive, loaned by Dutch Government specially for that occasion.

TYPES

1. Continuous wave Doppler
2. Pulsed wave Doppler
3. Color Doppler
4. Power Doppler
5. Contrast enhanced Doppler

CONTINUOUS WAVE DOPPLER

This ultrasound system detects Doppler shifted signals by continuous and simultaneous transmission and reception .Output from continuous wave Doppler is a mixture of Doppler frequency shifts from all targets within the sensitive region of Ultrasound beam .This is the simplest of all , but detects only the magnitude of change .The disadvantages of this system is that it does not give directional information and it is difficult to interpret due to confounding signals. This system is unable to distinguish between targets according to the range. This is no longer used in practice [23]

PULSED WAVE DOPPLER

This technique uses range gating, that is only signals from chosen depth alone are detected which reduces confounding and improves signal strength.

In this system, received signal is compared with the reference signal and depending on the degree of shift directional information is obtained. Output of pulsed wave Doppler is presented as a spectral wave form. Pulsed wave Doppler can be used in combination with gray scale imaging which is called as Duplex Doppler or in combination with color Doppler which is called as Triplex Doppler. In this system measurement of absolute velocity, ratios are possible. It provides directional information and helps in estimating degree of lesion also.[23]

DOPPLER COLOR IMAGING

This is a type of pulsed wave Doppler where Color coding is given to Doppler shift frequency.[23] It is tempting to view color Doppler images as depictions of vascular lumen similar to angiogram but they represent just Doppler shift frequency .The natural role of the color Doppler is to create a road map which can be used as a guide to locate the Doppler sample volume. The color map determines which color to be assigned to each shift. Traditionally flow towards the probe is coded red and flow away from the probe is coded as blue. It is helpful to detect turbulence and to find out deeply located, anatomically abnormal, small vessels. The disadvantages include the need to use with pulsed wave Doppler and its inability to find out the degree of the lesion.

POWER DOPPLER

This is a new generation Doppler which measures the amplitude of emitted signal than the frequency which is depicted by the conventional Doppler. It has good signal strength ,much improved sensitivity to flow hence visualizes even the smaller vessels. It displays as a single color map on superimposed gray scale. Its limitations are lack of velocity and directional information. It is useful as a guide to take peripheral samples [24]

CONTRAST DOPPLER

This recent technique uses echogenic contrast material, hence it depicts the vessel lumen well. It is also used to detect flow in small vessels beyond the limit of resolution. It is predominantly used in cardiovascular imaging. The usual contrast agents used are encapsulated nitrogen bubbles, perfluro octyl bromide, Albunex and Levovist [23]

INTERPRETATION

Results from Doppler is usually presented in three ways

1. Audible sounds
2. Spectral display
3. Color images

AUDIBLE SOUNDS

Doppler signal in real sense is a sound and the data potrayed by the color image and spectral display are no more than charecterisation. It is a reflection between the sound beam and series of targets in moving medium .In real scenario it is the characteristics of moving medium that changes the Doppler signal .For many years the clinical diagnosis using Doppler were made through trained ears. Today even with modern acquisition techniques and presentation in various formats, a seasoned practitioner still derives benefit from just listening to the sounds. Output from any type of Doppler can be represented in an audible fashion[23]

SPECTRAL WAVE FORM

The output from pulsed wave Doppler is presented in this form. This is produced by recording of different frequency shifts due to different velocity of moving objects .These frequency shifts are analyzed by Fast Fourier Transform analysis. Three variables are plotted in display in this wave form. Amplitude in vertical axis, frequency and time on horizontal axis. [24]

INTERPRETATION

Three important variables are analysed

1. Pattern of wave form
2. Frequencies and velocities
3. Derived indices

PATTERN OF WAVE FORM

Normal spectral wave form has an immediate systolic peak and plateau diastolic phase. A slow rising (parvus et tardus) pattern suggests the presence of renal artery stenosis.

FREQUENCIES AND VELOCITIES

A number of frequencies and velocities can be obtained from analysis of the Doppler spectral wave form. The commonly used are

FREQUENCIES

1. PSF (peak systolic frequency)
2. EDF (end diastolic frequency)
3. Mean frequency

VELOCITIES

1. PSV (peak systolic velocity)
2. EDV (end diastolic velocity)
3. Mean velocity

DERIVED INDICES

A list of derived indices from above mentioned velocities and frequencies are introduced to further improve the diagnostic utility of Doppler. These are used in specific circumstances.

1. RI (Resistive index)=PSV-EDV/PSV
2. PI (Pulsatility index)=PSV-EDV/mean V
3. S-D Ratio=PSV/EDV
4. B-A Ratio=EDV/PSV×100
5. AT (Acceleration time)-time to reach PSV in seconds
6. AI (Acceleration index)-slope of systolic curve/unit time

Of all the indices resistive index is the most commonly used index.[15] It is also called as Pourcelot index. The normal value is 0.58-0.64.In neonates it is high (0.7-1.0). It reaches the adult value by one year. Value more than 0.7 is generally considered abnormal. However it is a non specific index and elevated in many conditions.

CLINICAL APPLICATIONS

1. Obstruction
2. Renal artery stenosis

3. Diabetic nephropathy
4. Renal parenchymal disease
5. Reflux nephropathy
6. Acute renal failure
7. Renal transplantation
8. Progression
9. Dialysis access
10. Acute pyelonephritis
11. Renal colic

OBSTRUCTION

Animal studies have shown that renal obstruction increases renal vascular resistance and produce changes in the Doppler waveform. Platt JF. et al [2] studied the value of the resistive index calculated from the Duplex Doppler waveform to distinguish between obstructive and non obstructive pyelocaliectasis in 229 kidneys in 133 patients. There was a significant difference between the mean resistive index of the obstructed (0.77 +/- 0.05) and the non obstructed dilated (0.63 +/- 0.06) kidneys (p less than .01). Analysis of the receiver-operating-characteristic curve showed an resistive index of 0.70 to be a good discriminatory level for obstruction, with 92% sensitivity, 88% specificity, and an accuracy of 90%. All 109 normal kidneys had a resistive index less than 0.70. Use of duplex Doppler sonography should improve the specificity, and thus the accuracy of sonography in the noninvasive diagnosis of obstruction and should be used whenever a dilated collecting system is identified.

REFLUX NEPHROPATHY.

Kawauchi A et al [9] investigated the relationships of the renal resistive index, reflux and renal scarring. The resistive index in the interlobar artery was measured using power Doppler ultrasonography in 22 patients with reflux (reflux group), 13 with postoperative or resolved reflux (previous reflux group) and 20 normal people who served as controls. Resistive index values in 11 kidneys with mild or high grade reflux were significantly higher than in 22 with low grade reflux and in the 40 normal kidneys. The resistive index in the 11 kidneys with reflux and scarring was significantly higher than in the 22 with reflux and without scarring, and in the 40 normal kidneys. The resistive index in the 14 kidneys with previous reflux and scarring was significantly higher than in 12 with previous reflux and without scarring, and in the 40 normal kidneys. Receiver operating characteristics curve analysis in 25 kidneys with and 34 without scarring revealed that a discriminatory resistive index value of 0.71 was optimal for detecting renal scarring. When the resistive index cutoff value was 0.71, there was 76% sensitivity, 91% specificity and 85% overall accuracy to diagnose renal scarring. This study concluded that an elevated resistive index in kidneys with reflux predicts renal scarring.

DIALYSIS ACCESS

Grogan J et al[26] investigated arteriovenous fistula′s with color duplex ultrasound surveillance 4 to 12 weeks postoperatively to identify hemodynamically significant abnormalities that may contribute to access failure. 54 upper extremity arteriovenous fistula′s were subjected to color Doppler assessment before access. A peak systolic velocity ratio of >/=2:1 was used to detect >/=50% stenosis involving arterial inflow and venous outflow, whereas an systolic velocity ratio of >/=3:1 was used to detect >/=50% anastomotic stenosis. Color Doppler findings were compared with preoperative vein mapping and postoperative fistulography when available. The sensitivity, specificity, and accuracy of color Doppler in detecting access stenosis >/=50% were 93%, 94%, 97%, respectively. Color flow Doppler provides accurate imaging and access flow volume measurement of the hemodialysis vascular access. It can readily identify subsets of patients at high risk for future thrombosis. It is noninvasive, can be done at bedside, hence allows convenient evaluation at the dialysis facility. In Europe, [39] Doppler ultrasound has become the standard of care for evaluation of arteriovenous fistula dysfunction and is essential in the preoperative evaluation for access placement. It also can diagnose the arterial inflow disease that has become more prevalent in our aging, diabetic, end-stage renal disease population. Access management programs based on Doppler ultrasound have been highly successful and have produced outcome data as good or better than provided with other techniques. In conclusion, Doppler ultrasound should be included as a part of an integrated vascular access management program.

ACUTE CHILDHOOD PYELONEPHRITIS.

In the absence of specific symptomatology in children, the early diagnosis of acute pyelonephritis is a challenge, particularly during infancy. In an attempt to differentiate acute pyelonephritis from lower urinary tract infection , Halevy R et al [33] evaluated the ability of power Doppler Utrasonography to predict renal parenchymal involvement, as assessed by dimercaptosuccinic acid (99m) Tc-DMSA) scintigraphy. The study comprised 62 patients, 46 girls and 16 boys, aged 2 weeks to 5 years, admitted to the pediatric department with febrile urinary tract infection. All children were examined by power Doppler and DMSA scintigraphy within the first 3 days of admission. In the group of 31 patients with one or more DMSA scan abnormalities, the power Doppler showed a matching perfusion defect in 27 (87%). Of 26 children with normal DMSA scintigraphy, the power Doppler evaluation was also normal in 24. The sensitivity and specificity of power Doppler for the detection of affected kidneys were 87% and 92.3%, and the positive predictive value and negative predictive value were 93.1% and 85.7%, respectively. These data indicate that the power Doppler has a high sensitivity and specificity for differentiating acute pyelonephritis from lower urinary tract infection and may be a useful and practical tool for the diagnosis of acute pyelonephritis in infants and children.

ACUTE RENAL FAILURE.

Imaging techniques, especially ultrasonography and Doppler, can give an effective assistance in the differential diagnosis of acute renal failure . Nori G et al [28] proposed that an resistance Index value >0.75 is reported as optimal in attempting differential diagnosis between acute tubular necrosis and pre renal acute renal failure. However in hepato renal syndrome the resistive index is elevated.

Izumi et al [4] reported the utility of Doppler Ultrasound in differentiating pre renal azotemia from established acute tubular necrosis. 40 patients with oliguric acute renal failure underwent Doppler and resistive and pulsatility indices were measured from segmental arteries. For all patients with normal resistive and pulsatility index , the fractional excretion of sodium was <1 at the onset of acute renal failure. In those with elevated resistive and pulsatility indices, these indices declined to baseline in those recovered from acute tubular necrosis. Thus Doppler helpful in diagnosis of established acute tubular necrosis as well as to predict recovery

RENAL COLIC

Geavlete P et al[40]investigated the value of duplex Doppler ultrasonography in patients with renal colic. In this study the resistive index , difference of the resistive index and Duplex Doppler intravesical recording (ureteral jets) were compared with renographic findings in patients with renal colic . He studied 377 cases with suspected renal colic by intravenous pyelography ,grey-scale ultrasonography and Duplex Doppler with determination of the resistive index , the difference between the resistive index of ipsilateral and contralateral kidneys and the amplitude(maximum length of the intravesical ureteral jet), velocity and frequency of the urine bolus. The difference in resistive index in patients with obstruction was significantly higher than in patients with normal both kidneys, at 0.08 (0.05) and 0.001 (0.03), respectively ($P < 0.001$). The resistive index was 75.5% sensitive and 92.5% specific and difference in resistive index was 80.7% sensitive and 95.7% specific versus IVP, considered the reference value . The presence of the intravesical ureteral jets of the renal colic side, associated with the values of resistive index (Resistive index < or = 0.70) and delta resistive index (delta resistive index < or = 0.06), was followed by spontaneous passage of the stones in 71% of cases. Renal Duplex Doppler and consecutively, intravesical evaluation of ureteral jets could detect acute obstruction and as a functional investigation, could have a predictive value regarding the ureteral stones passage. It could replace the intravenous pyelogram being a sensitive and highly specific test.

Pepe P et al [31] evaluated if the addition of a renal color-doppler ultrasonography in the setting of acute renal colic improves the sensitivity of conventional sonography.100 patients with renal colic underwent color Doppler evaluation of three different parenchymal areas, ureteric jets in response to hydration. A renal resistive index >0.70 and/or a 10% difference between the kidneys were considered as diagnostic of obstructive uropathy. An asymmetric and/or reduced ureteric jet from the ureteric orifices was an additional indicator of obstruction. All patients underwent a CT scan both with and without the administration of contrast medium. Enhanced helical CT demonstrated an urinary stone in 90 out of the 100 patients (90%): 29 at pelvis, 28 at the pelvi-ureteral junction, 23 in lumbo-iliac region and 10 juxtavesical stones. Among 90 patients with urolithiasis, the stone was undetectable with ultrasound in 11 cases(12.2%) , in 8 cases (8.9%) pyelocalicectasis was absent, and in 6 patients (6.6%) a non-obstructive hydronephrosis was present. Median resistive index in obstructed and non-obstructed kidney was 0.73 (range 0.71-0.87) versus 0.62 (0.50-0.68) respectively. In two obstructed kidneys the resistive index was <0.70 but greater than 10% compared with normal side. Sensitivity and specificity of ultrasound, Color Doppler (Resistive index +ureteric jet), unenhanced helical CT and Color Doppler in association with unenhanced helical CT were 94.8% and 5.5%, 98.9% and 90.9%, 100% and 100%, respectively. Color Doppler in patients with renal colic and/or pelvicalicectasis improves the diagnostic accuracy of ultrasound in distinguishing between obstructive and non-obstructive dilatation,

RENAL ARTERY STENOSIS

Ultrasonographic detection of renal artery stenosis can be made with a sensitivity and specificity exceeding 90% by an experienced investigator [5.] A combination of Doppler parameters making use of both direct and indirect signs of stenosis should be used. The reversibility of hypertension or impaired renal function (i.e. the presence of renovascular hypertension or azotemia) after successful correction of renal artery stenosis can be assessed by measuring segmental artery resistance indices. A resistance index value greater than 0.80 makes a treatment effect highly unlikely, and these patients should not undergo angioplasty or surgery of their stenosis [37].

Bolduc JP et al [30] evaluated and compared the relative cost-benefit of Doppler sonography, Magnetic resonance angiography, and captopril-enhanced renal scintigraphy as techniques for predicting a patient's clinical response to renal angioplasty. Doppler sonography is more cost-efficient but less sensitive than MR angiography for identifying patients with renovascular hypertension. Hence he concluded that magnetic resonance angiography should be favored in hypertensive patients who are resistant to medical therapy to avoid false-negative examinations.

His observations were confirmed by another investigator. Demirpolat G et al [36] retrospectively evaluated false-negative results of Doppler sonography in the diagnosis of renal artery stenosis using intrarenal criteria. Mean intrarenal acceleration and acceleration time obtained directly from color Doppler sonography and findings of angiographic examination of the stenotic renal arteries were evaluated. During the study period, 5 cases of renal artery stenosis had been angiographically confirmed in 46 patients (25 male and 1 female; mean age, 50 +/- 19 years [+/- standard deviation]). Mean intrarenal arterial acceleration, acceleration time or both were abnormal in 42 kidneys (76%) (group A) and normal in 13 kidneys (24%) (group B). The mean age +/-standard deviation was significantly higher for patients in group B (60 +/- 12 years) than for those in group A (47 +/- 20 years) ($p > 0.05$). In group B, most of the stenotic lesions were atherosclerotic, and in all kidneys but one the lesions were located at the renal ostium or the proximal half of the artery. Isolated use of intrarenal Doppler sonographic criteria for renal artery stenosis may lead to an unacceptably high incidence of false-negative results in the diagnosis of this condition especially in elderly patients.

Doppler is not only useful to diagnose renal artery stenosis but also useful to predict the outcome .It is a known fact that not all patients with renal artery stenosis will benefit from angioplasty or surgery. For this reason it is not sufficient to diagnose the presence of renal artery stenosis, but one also has to evaluate its functional significance. Doppler ultrasonography can be used to predict the outcome of therapy for renal-artery stenosis. Radermacher J [37]et al evaluated whether a high level of resistance to flow in the segmental arteries of both kidneys (indicated by resistance-index values of atleast 80) can be used prospectively to select appropriate patients for treatment.

He evaluated 5950 patients with hypertension for renal-artery stenosis using color Doppler ultrasonography and measured the resistance index. Of this 5950 patients 138 patients diagnosed to have either unilateral or bilateral renal artery stenosis of more than 50 percent of the luminal diameter . All the 138 patients underwent either renal angioplasty or surgery and the procedure was technically successful in 131 (95 percent). Creatinine clearance and 24-hour ambulatory blood pressure were measured before renal-artery stenosis was corrected , 3, 6, and 12 months after the procedure and yearly thereafter. The mean (+/-SD) duration of follow-up was 32+/-21 months. Among the 35 patients (27 percent) who had resistance-index values of at least 80 before revascularization, the mean arterial pressure did not decrease by 10 mm Hg or more after revascularization in 34 (97 percent). Renal function declined (defined by a decrease in the creatinine clearance of at least 10 percent) in 28 (80 percent); 16 (46 percent) became dialysis dependent and 10 (29 percent) died during follow-up. Among the 96 patients (73 percent) with a resistance-index value of less than 80, the mean arterial pressure decreased by at least 10 percent in all but 6 patients (6 percent) after revascularization; renal function worsened in only 3 (3 percent), all of whom became dialysis dependent and 3 patients (3 percent) died during follow up ($P<0.001$ for the comparison with patients with a resistance-index value of atleast 80). A renal resistance-index value of at least 80 reliably identifies patients with renal-artery stenosis in whom angioplasty or surgery will not improve renal function, blood pressure, or kidney survival.

TRANSPLANTATION

Drudi FM et al [46] assessed the role of Ultrasound , Color Doppler and Power Doppler in the diagnosis and in the follow-up of renal graft pathology by evaluating morphological and functional features of the vasculature and comparing these to other clinical parameters. Four hundred and thirty-six renal allograft recipients underwent periodical ultrasound , color and power Doppler to evaluate morphology and perfusion of the graft. Resistive index and pulsatility index were measured in order to monitor the flow variations from the renal to the arcuate arteries. Power Doppler was used mainly to study the morphology of the cortical vessels. Statistical analysis demonstrated the efficacy of this method in the differentiation between normal and pathological grafts, but there was a reduced statistical difference between the two pathological groups. Histological analysis performed on 87 patients (20%) showed good correlation with resistive index. Color Doppler is a non-invasive diagnostic method which provides flow-metric quantitative parameters for the hemodynamic assessment of the renal transplant. These values present a certain sensitivity but are not specific of any specific cause of allograft dysfunction, as there is no reliable differentiation between acute rejection and other parenchymal pathologies. During the follow-up, resistive and pulsatility indices had no predictive value. Resistive inndex variations from renal artery to cortical vessels (hilum-cortical ratio) showed a good correlation with the clinical evolution of the transplant

TRANSPLANT RENAL ARTERY STENOSIS.

Over a 3-year period, . Radermacher J et al evaluated patients who were referred for investigation of possible transplant renal artery stenosis. He investigated the following parameters: peak systolic velocity in the external iliac and renal arteries, acceleration time , acceleration index in the intrarenal arteries, acceleration time in the renal artery, resistance index, and the ratio of the peak systolic velocity in the renal and external iliac arteries. He also used Magnetic resonance angiography and digital subtraction arteriography to verify the degree of stenosis. After these evaluations, the patients were classified into 2 groups, 1 with and the other without significant stenosis (> 50% narrowing of the lumen) on digital subtraction arteriography. He also included a control group of patients who had undergone renal transplantation at least 6 months before and had a good course after transplantation, a diastolic blood pressure of 90 mm Hg or less, and were taking a maximum of one antihypertensive drug. The study population consisted of 22 patients suspected to have transplant renal artery stenosis (10 without and 12 with confirmed significant stenosis) and 19 control patients. He found statistically significant differences between the mean values of these 3 groups except for the peak systolic velocity in the iliac artery and the resistance index in the intrarenal arteries. The most accurate parameters to diagnose transplant renal artery stenosis were an acceleration time of 0.1 second or higher in the renal and intrarenal arteries, a peak systolic velocity of greater than 200 cm/second in the renal artery, and a ratio of peak systolic velocity in the renal and external iliac arteries of greater than 1.8. He concluded that Duplex Doppler sonography was an excellent method of screening for patients suspected to have transplant renal artery stenosis and can help to select which of those patients should undergo digital subtraction arteriography.

THE RESISTANCE INDEX AND RENAL ALLOGRAFT SURVIVAL.

Radermacher J et al [8] tested whether a renal arterial resistance index of less than 80 was predictive of long-term allograft survival. The renal segmental arterial resistance index was measured by Doppler ultrasonography in 601 patients at least three months after transplantation . All patients were followed up for three or more years. The combined end point was a decrease of 50 percent or more in the creatinine clearance , allograft failure (indicated by the need for dialysis), or death. A total of 122 patients (20 percent) had a resistance index of 80 or higher. Eighty-four of these patients (69 percent) had a decrease of 50 percent or more in creatinine clearance, as compared with 56 of the 479 patients with a resistance index of less than 80 (12 percent); 57 patients with a higher resistance index (47 percent) required dialysis, as compared with 43 patients with a lower resistance index (9 percent); and 36 patients with a higher resistance index (30 percent) died, as compared with 33 patients with a lower resistance index (7 percent) ($P<0.001$ for all comparisons). A total of 107 patients with a higher resistance index (88 percent) reached the combined end point, as compared with 83 of those with a lower resistance index (17 percent, $P<0.001$). The multivariate relative risk of graft loss among patients with a higher resistance index was 9.1 (95 percent confidence interval, 6.6 to 12.7). Proteinuria (protein excretion, 1 g per day or more), symptomatic cytomegalovirus infection, and a creatinine clearance of less than 30 ml per minute per 1.73 m2 of body-surface area after transplantation were associated with increased the risk of graft loss. He concluded that a renal arterial resistance index of 80 or higher measured at least three months after transplantation is associated with poor subsequent allograft performance and death.

RENAL DOPPLER RESISTANCE INDICES ARE ASSOCIATED WITH SYSTEMIC ATHEROSCLEROSIS IN KIDNEY TRANSPLANT RECIPIENTS.

Heine GH. et al [43] investigated 105 renal transplant recipients, intrarenal resistive index and pulsatility index were measured in segmental arteries at five representative locations. For assessment of sub clinical atherosclerosis, common carotid intima-media thickness, and ankle-brachial blood pressure index were determined. Transplant recipients with high coronary risk had higher intrarenal resistance indices than low-risk patients. Higher age, female gender, and lower body mass index were independently associated with increased resistance indices. Renal resistance indices were correlated with common carotid intima-media thickness [RI: $r= 0.270$ ($P= 0.005$); PI: $r= 0.355$ ($P < 0.001$)]. This association remained significant even after adjusting for renal function. Renal resistance indices were increased in patients with pathologic ankle-brachial-indices compared to patients with physiologic ankle-brachial-indices [RI: 73.3 +/- 7.1 vs. 70.2 +/- 6.9 ($P= 0.03$); PI: 146.4+/- 29.9 vs. 131.4 +/- 25.9 ($P= 0.01$)].

Renal resistance indices were neither significantly correlated with glomerular filtration rate , nor with donor age. Intra renal resistance indices are associated with traditional cardiovascular risk factors as well as with subclinical atherosclerotic vessel damage and thus should not be considered as specific markers of renal damage.

DETECTION OF CHRONIC ALLOGRAFT NEPHROPATHY

Nankivell BJ [38] et al evaluated a new technique of color Doppler quantification for diagnosis of chronic allograft nephropathy . The maximal fractional area (systolic color pixels / total area) was 28.7+/-9.7% in normal subjects and reduced to 18.8+/-8.0% in grade 1 and 12.5+/-6.4% in grade 2 chronic allograft nephropathy (both P<0.001). The minimum color fractional area was reduced from 10.3+/-5.3% in normal subjects to 3.1+/-2.6% in grade 2 chronic allograft nephropathy (P<0.001), but was less useful. Distance from peripheral color pixels to capsule increased in chronic allograft nephropathy grade 2 versus 0 (6.0+/-1.6 vs. 3.9+/-1.0 mm, respectively ;P<0.001). Calcineurin inhibitor nephrotoxicity reduced maximal fractional area (18.0+/-9.3 vs.26.9+/-10.7%; P<0.001) and other dynamic measurements. Parenchymal damage exerted minimal effect on resistance index, mean variance, and peak Doppler velocity. Maximal fractional area (cutoff<17.3%) was 69% sensitive, 88% specific to diagnose chronic allograft nephropathy and 87% sensitive, 71% specific to diagnose severe chronic allograft nephropathy . Distance to capsule of >5 mm was less sensitive (49%) but more specific (91% alone, and 97% combined with maximal fractional area).

DIABETIC NEPHROPATHY

Casadei A et al [42] investigated the role of the resistive index in of 160 type 2 diabetic subjects and divided them into 4 groups according to the severity of diabetic nephropathy. The measurement of resistive index was useful to detect a subgroup of 28 subjects (43.8%) among patients in the early stages of diabetic nephropathy (64 patients of group 1), showing resistive index values equal to or above the threshold value of 0.7. The determination of renal size and of renal parenchyma echogenicity proved to be of little value. The most relevant clinical information is provided by the resistive index, a parameter that will allow the early detection of patients affected by type 2 diabetes, who show renal vascular involvement without however any other alterations of the traditional ultrasound parameters.

MEASUREMENT OF TOTAL AND SPLIT RENAL FUNCTION.

Yura T et al [7] evaluated total and split renal functions from the pattern for renal arterial blood flow detected by ultrasound Doppler in healthy subjects and patients with varying degrees of renal dysfunction due to disorders other than renovascular hypertension or severe aortic valvular disease.. The ratio of peak diastolic to systolic velocity correlated well with both p-aminohippurate clearance and creatinine clearance. Acceleration time was correlated with the clearance of neither compound. To evaluate the clinical usefulness of ultrasound Doppler in the assessment of split renal function, he compared the diastolic to systolic velocity ratio with the renal function obtained by radionuclide methods. The split renal glomerular filtration rate, calculated by a method which makes use of the early renal uptake of 99mTc-diethylenetriamine pentaacetic acid, correlated well with the diastolic to systolic velocity ratio. These results indicate that the ultrasonic measurement of renal arterial blood flow by the pulsed Doppler method may be useful for assessment of total and split renal function.

RENAL PARENCHYMAL DISEASE

Argalia G et al [45] investigated the role of Doppler parameters to differentiate glomerular disorders from those with vascular or tubulointerstitial involvement. 32 patients with clinical and laboratory signs of medical renal disease were examined with color Doppler. The resistive index was calculated from the Doppler waveform signal. The resistive index values were compared with renal biopsy findings, serum creatinine levels and clinical and laboratory variables such as hematuria and proteinuria. Doppler demonstrated a normal resistive index value in 17/18 patients with glomerulonephritis (mean value: 0.59 +/- 0.05). In only one patient , even though biopsy indicated the involvement of only one glomerulus (membranous nephropathy II stage), resistive index was high i.e.,0.79. In 4 patients with simultaneous glomerular and interstitial involvement, the mean resistive index value was 0.17 +/- 0.01. In the 10 cases of tubulointerstitial or vascular disease , the resistive index was 0.83

+/- 0.07. As far as the correlation between serum creatinine levels and resistive index was concerned, in 8 patients with high values (1.5-8mg/dl), the mean resistive index was 0.72 +/- 0.08 and only a weak correlation was found between the resistive index and the degree of renal failure as expressed by serum creatinine levels.. Doppler Ultrasound seems to be capable of characterizing renal parenchymal disease , distinguishing glomerular from vascular or tubulointerstitial involvement.

Platt JF, et al [20]compared conventional and Doppler ultrasound with clinical and biopsy parameters used to assess disease activity and outcome in lupus nephritis and to assess the predictive value of Doppler . Thirty-four patients with lupus nephritis prospectively underwent laboratory and Doppler ultrasound analysis at the time of renal biopsy. The ultrasound parameters were renal length, relative echogenicity, and resistive index . Laboratory parameters were serum creatinine level, urinary protein level, and serum markers of disease activity. Biopsy parameters were activity index, chronicity index, and assessment of the tubulo-interstitium of the kidney. Follow-up data were obtained in all patients for at least 1 year. Ten patients with elevated resistive index (>0.70) had significantly ($p < .05$) higher chronicity indices and creatinine levels than the 24 patients with a normal resistive index. Resistive index correlated significantly ($p < .05$) with creatinine level, chronicity index, and presence of interstitial disease. Only resistive index and chronicity index were statistically significant predictors of a poor renal outcome. Abnormalities at conventional US were not predictive of renal outcome. A normal resistive index predicted a better renal outcome whether or not creatinine level was elevated. Renal Doppler ultrasound may be of greatest clinical utility, by allowing identification of patients with higher likelihood of subsequent improvement or worsening of renal status.

Mostbeck GH et al[13] evaluated the histopathologic changes influencing Doppler measurements of the resistive index in renal arteries in renal parenchymal diseases, 68 kidneys in 34 consecutive patients with various forms of renal parenchymal diseases were studied by duplex Doppler ultrasound immediately before percutaneous renal biopsy. The resistive index , renal length, and renal cortical echogenicity were correlated with the amount of glomerular, interstitial, and vascular changes graded on a scale from 0 to 100. The renal vascular resistance and therefore the resistive index are significantly correlated with the prevalence of arteriolosclerosis, glomerular sclerosis, arteriosclerosis, edema, and focal interstitial fibrosis. There was no significant difference of the resistive index in five groups of different renal parenchymal diseases. Of 34 patients, 24 presented with an resistive index less than 0.7, which was thought to be within the normal range so far. Additionally, the resistive index increases as the patient's age increases, due to higher incidence of arteriosclerosis. Quantitative duplex ultrasound using the resistive index does not reliably distinguish different types of renal medical disorders.

Galesic K et al [29] evaluated renal vascular resistance in patients with glomerular diseases by measuring resistive index and to correlate it with renal function. The Doppler parameters were also correlated with histopathological findings in the kidney which underwent the percutaneous biopsy. Duplex Doppler sonography was used to measure resistive index in intra renal arteries in 50 patients with glomerular diseases and 60 age-matched control subjects.. The mean resistive index in 50 patients with glomerular diseases was 0.68 +/- 0.09, which was statistically significantly higher than in 60 control subjects (the mean resistive index was 0.596 +/- 0.035). In a group of patients with membrano proliferative glomerulonephritis the mean resistive index was 0.817+/- 0.624 which was statistically significantly higher than in other groups of glomerulonephritis. The renal resistance index significantly correlated with serum creatinine, creatinine clearance and beta 2 microglobulin clearence. Qualitative duplex sonography measure of renal arterial resistive index does not appear to be reliable in distinguishing different types of glomerulonephritis.

Platt JF et al [2] calculated the resistive index from the duplex Doppler waveform, compared it with clinical and laboratory findings and the results of renal biopsy in 41 patients with non obstructive (medical) renal disease. Kidneys with active disease in the tubulointerstitial compartment had a mean resistive index of 0.75 +/- 0.07.This was statistically significantly different (p less than .01) from the resistive index in kidneys with disease limited to the glomeruli (mean resistive index of 0.58 +/- 0.05). Acute tubular necrosis resulted in an elevated resistive index (mean resistive index = 0.78 +/- 0.03) as did vasculitis (mean resistive index = 0.82 +/- 0.05. There was a weak correlation between serum creatinine level and resistive index value, reflected by a linear correlation coefficient of 0.34. In patients with normal renal resistive index, the mean creatinine level was 1.7 +/- 1.7, whereas in those with abnormal resistive index values (greater than or equal to 0.70), the mean creatinine level was 3.7 +/- 3.6. The production of Doppler waveform changes is strongly influenced by the site of the main disease within the kidneys. Active disease within the tubulointerstitial compartment (acute tubular necrosis, interstitial nephritis)or vasculitis generally resulted in an elevated resistive index, whereas disease limited to the glomeruli, no matter how severe it was, did not significantly elevate the resistive index .

Sugiura T et al [14] investigated whether Doppler ultrasonography in glomerular diseases could discriminate tubulointerstitial lesions, which correlated closely with long-term renal function. Sixty patients with primary or secondary glomerular diseases were examined by Doppler ultrasonography immediately before renal biopsy. The resistive index was calculated, as was the atrophic index (a newly proposed parameter defined as renal sinus length/renal length). These were compared with histologic changes in biopsy specimens. Receiver operator characteristic analysis showed a resistive index of 0.65 to be the optimal for discriminating tubulointerstitial changes with specificity of 100% and sensitivity of 57.1%. Tubulointerstitial injury scores were significantly higher in patients with resistive indices exceeding 0.65 than in patients with a lower value. An atrophic index of 0.70 was also shown to be optimal with specificity 100% and sensitivity 61.9%. In combination, the two indices showed improved sensitivity; when the patients were divided into groups where both resistive and atrophic indices were normal (respectively $<$ or $=$ 0.65 and $<$ or $=$ 0.70) or where either or both were high, sensitivity rose to 85.7%, while specificity remained 94.4%. . In combination, the resistive and atrophic indices discriminated tubulointerstitial injury in glomerular diseases with high specificity and sensitivity.

Hence at the moment the role of Doppler in glomerular diseases remains controversial. Although most studies show encouraging results [2,20,45] some are disappointing [13,29].The correlation between serum creatinine and resistive index is weak although few studies support that observation too.[20,29]

Generally it is renal vasculitis and tubular-interstitial nephropathies which are more frequently identified by conventional Ultrasound and Doppler than glomerulonephritis and the proposed reason for that observation being glomerular component accounting only for 8% of the renal parenchyma, whereas the highest percentage is occupied by vascular and tubulo-interstitial component.

PREDICTIVE VALUE OF RESISTIVE INDEX IN CHRONIC NEPHROPATHIES

Splendiani G et al [11] tried to discover if resistive index represents a prognostic index of progressive renal failure. To this purpose he compared renal resistive index and serum creatinine obtained from 28 patients at diagnosis , with serum creatinine values after a 3-year follow-up period. Using a linear regression test, he found a strong correlation between the initial value of resistive index and the value of creatinine variation (p = 0.006). All of the patients with normal resistive index at the beginning maintained a stable renal function. Conversely, the patients with high resistive index at their first control showed a progressive renal failure. This study shows the reliability of resistive index in the prognostic evaluation of renal outcome.

Radermacher J et al [16] prospectively tested the hypothesis that a high renal resistance index (≥80) predicts progression of renal disease in patients without renal artery stenosis. In 162 patients newly diagnosed with renal disease, the resistance index (1-[end diastolic velocity/maximum systolic velocity]*100) was measured in segmental arteries of both kidneys. Creatinine clearance was measured at baseline, at 3, 6, and 12 months, and then at yearly intervals thereafter (mean follow-up 3±1.4 years). The combined endpoint was a decrease of creatinine clearance by ≥50%, end-stage renal disease or death. Of the twenty-five patients (15%) had a renal resistance index value ≥80 at baseline, nineteen (76%) had a decline in renal function; 16 (64%) progressed to dialysis, and 6 (24%) died. In comparison, in patients with renal resistance index values <80 at baseline , 13 (9%) had a decline in renal function, only 7 (5%) became dialysis-dependent, and 2 (1%) died ($P<0.001$). In a multivariate regression analysis, only proteinuria and resistance index were independent predictors of declining renal function. A renal resistance index value of ≥80 reliably identifies patients at risk for progressive renal disease.

To conclude from both above mentioned studies [11,16] renal resistance index measured by Doppler can be used as a prognostic tool to predict patients at risk of progression at diagnosis. Whether intensification of therapy in patients with high baseline resistive index will decrease the risk of progression is an area that requires further research

MATERIALS & METHODS

A total of 75 patients underwent Doppler examination of both kidneys immediately before percutaneous needle biopsy. The criteria adopted for biopsy were :

1. Proteinuria >1 g/day
2. Proteinuria >0.5g/day with hematuria
3. Hematuria with RBC casts
4. Rapidly worsening renal function

71 patients found to have glomerular disease after biopsy were included in the study. Rest of the four had interstitial nephritis or hypertensive nephrosclerosis were excluded. Renal biopsies were performed under ultrasound guidance with spring loaded automated biosy gun needle. (C.R.BARD 22mm) from the lower pole of the left kidney.

Data regarding age, sex, serum creatinine, 24hr urine protein, Body Mass Index, presence or absence of microhematuria, hypertension, renal failure were noted. Glomerular filtration rate was calculated by the Cockcroft-Gault formula.

DOPPLER ULTRASOUND

Doppler was performed just before the renal biopsy. A real time ultra sound device with color Doppler capacity was used (Toshiba medical ,Japan). The highest frequency that gave measurable wave form was used , supplemented by color or power Doppler as and when required for vessel localization.

After observation of intra renal arteries arcuate arteries located on cortico medullary junction were insonated using a 2-4 mm Doppler gate. Wave forms then optimized for measurement using lowest pulse repetition frequency without aliasing (to maximize wave form size), highest gain without obscuring background noise & lowest wall filter. 3- 5 measurable wave forms from each kidney were obtained and resistive index was measured from mean of the above values. We used the data from left kidney but no statistical difference was noted between both kidneys. (Data not shown). Resistive index was calculated as follows =Peak Systolic Velocity-End Diastolic Velocity/Peak Systolic Velocity[15]

To measure atrophic index the maximum longitudinal axis was considered as renal length . The major axis of outer boundary of renal sinus was taken as sinus length. The atrophic index was calculated as sinus divided by renal length to quantitate the atrophic changes in the renal parenchyma[14]

All measurements were made by a single observer unaware of study protocol.

HISTOLOGIC ANALYSIS

The biopsy specimens were studied by light and immunofluorescence microscopy to determine the pathologic diagnosis and to quantify the severity of histologic damage. For light microscopy tissues were fixed in Bouin solution and embedded in paraffin. Tissues cut as 2 μm sections & stained with Eosin and Haematoxylin , Periodic acid –Schiff and Silver. For Immunofluorescence anti sera against IgA,M,G,C1q,C3 were used.

A semiquantitative score was used to determine the extent of glomerulosclerosis & tubulo interstitial injury as studied previously[17]. Scoring was done by a single observer unaware of study protocol.

1. Quantification of tubulo interstitial disease:

Tubulo interstitial injury was scored semi quantitatively on 30 cortical fields of Eosin & Hematoxylin stained specimens with a 20 x objective.

Tubulo interstitial injury was defined as presence of tubular dilatation, tubular atrophy, sloughing of tubular epithelial cells or tubular basement membrane thickening.

0-no injury

1+ -<25%

2+-25-50%

3+-51-75%

4+->75%

2. Glomerular scoring

Glomerulo sclerosis is defined as glomeruli exhibiting segmental or global collapse of glomerular capillaries with or without associated hyaline deposition & adhesion of capillary tuft to Bowman's capsule. Glomerular score was obtained by multiplying severity of damage by the percentage of glomeruli with degree of injury.

STATISTICAL ANALYSIS

Statistical analysis was carried out using the SSPS soft ware (SSPS version 10.0, SSPS Inc). Results are shown as mean ± SD. Sensitivity and specificity were determined from a series of 2x2 tables in which tubulo interstitial injury and no injury represented in one axis, resistive index and atrophic index represented in the other. Tubulo interstitial score of 0 represent no injury and 1-4 were considered as its presence. After the sensitivity & specificity of each cut-off point was available a ROC (RECEIVER OPERATOR CHARACTERISTICS) curve[19] was plotted with ordinate indicating sensitivity, abscissa representing 1-specificity.The resultant ROC curve described the diagnostic efficacy of the test.

Progression was defined as >50% rise in serum creatinine form baseline . To asses the differences between groups unpaired‘t’ test, chi-square test or Fishers exact test were used as appropriate. Odds ratios for worsening renal function for various risk factors were calculated by 2X2 contingency table.

For multivariate analysis the effects of age, sex, renal failure at diagnosis, hypertension, proteinuria, Body Mass Index , smoking, Left ventricular Hypertrophy, Resistive and atrophic indices on progression were investigated .

RESULTS

71 subjects diagnosed to have glomerular disease were included.

		Mean ± SD
1	Age	34.49 5.68 yrs
2	Sex	31(43.7%) males
3	24 hr urine protein	2.63± 0.99 g/day
4	Creatinine	2.26 ± 0.84 mg/dl
5	GFR	50.25± 25 ml/min
6	Albumin	3.1± 0.7 g/dl
7	Cholesterol	213 ± 52 mg
8	Microhematuria	43%
9	Hypertension	40.8%
10	Nephrotic syndrome	19.7%
11	Renal failure at onset	43.66%

BIOPSY DETAILS

Minimal Change Nephropathy	5
Membranous Nephropathy	8
Mesangial proliferation	8
IgA Nephropathy	10
Focal Segmental Glomerulo Sclerosis	8
Diffuse Proliferative Glomerulo Nephritis	8
Membrano Proliferative Glomerulo Nephritis	4
Class IV Lupus Nephritis	9
Class III Lupus Nephritis	2
Class II Lupus Nephritis	2
Crescentic Glomerulo Nephritis	5

RECEIVER OPERATOR CHARACTERISTICS ANALYSIS

ROC (receiver operator characteristics) method[19] was used to determine whether resistive index could discriminate between no tubulo interstitial injury and its presence. In ROC analysis sensitivity and specificity were calculated for every score. An ideal test has an ROC that rises at critical score(indicating high sensitivity and specificity) and maintains plateau for higher values.

The entire range of resistive index in the study (0.47-0.83) was evaluated for predictive ability by ROC analysis. The ROC curve indicated that resistive index value 0.605 was the optimal value for discriminating tubulo interstitial injury with sensitivity of 82.7% and specificity of 92% . As the cut off point was raised the sensitivity improved at the expense of the specificity.

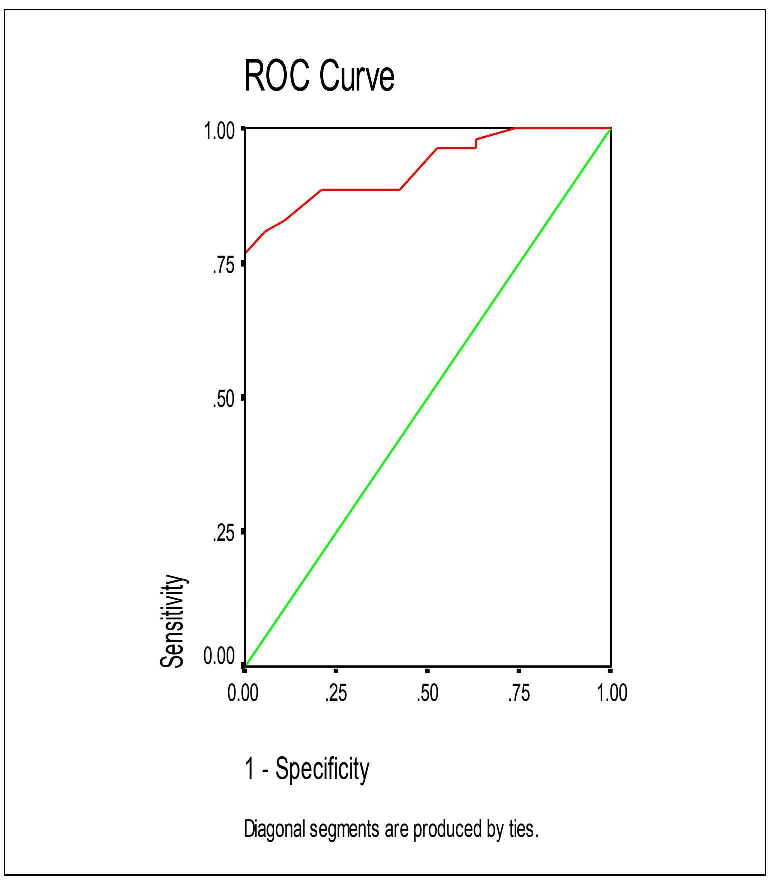

Fig-1. ROC curve of the predictive value of resistive index for discriminating the tubulointerstitial lesion. The receiver operator characteristics curve indicated that a resistive index of 0.65 was the optimal value for discriminating tubulo interstitial injury with 82.7% sensitivity and 92% specificity

ATROPHIC INDEX

Atrophic index was a new parameter proposed to evaluate the degree of atrophic changes in renal parenchyma[14]. As with resistive index the full range of atrophic index (0.53-0.76) was evaluated for the predictive ability in discriminating tubulointerstitial injury by ROC. The ROC indicated that AI of 0.65 had 69.2% sensitivity and 85%specificity.

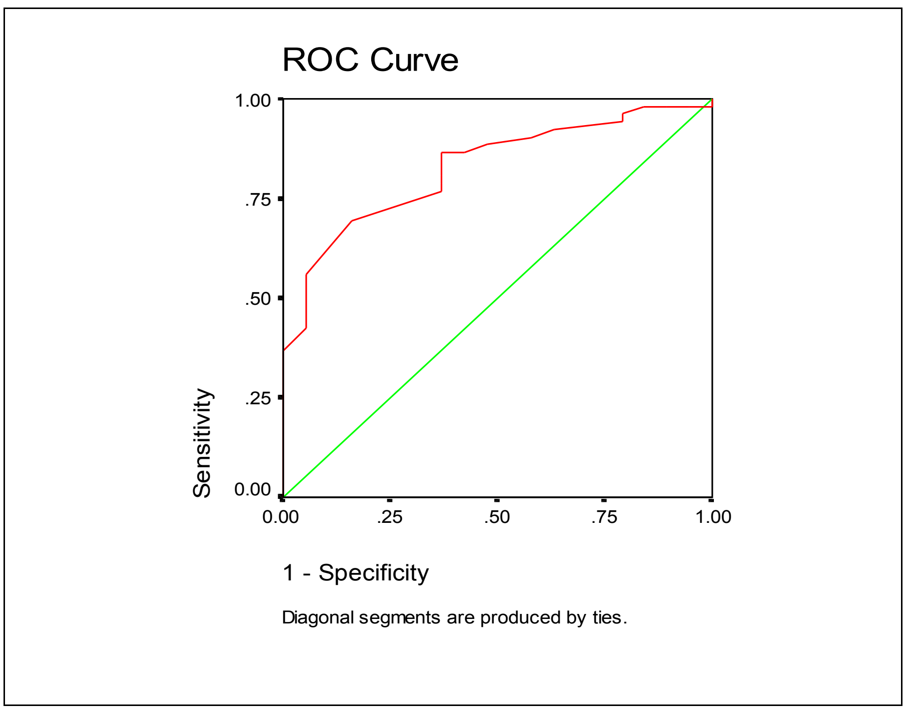

Fig - 2. ROC curve of the predictive value of atrophic index for discriminating the ubulointerstitial lesion. The receiver operator characteristics curve indicated that an atrophic index of 0.65 was the optimal value for discriminating tubulo interstitial injury with 69.2% sensitivity and 85% specificity .

RESISTIVE INDEX AND HISTOLOGIC CHANGES

Several studies have shown that a mean resistive index of people without preexisting renal disease was 0.60± 0.01 [2,15, 22].The mean resistive index of our healthy population was 0.58 ± 0.03(109 subjects).In general it is widely accepted that a resistive index of 0.7 is distinctly high[15]. Exceptions to this are children<4 yrs, adults>60 yrs.

Based on this the study group were divided into

<0.6 – normal

0.6-0.69 - high normal

>0.7- high

This was correlated with degree of tubulo interstitial injury

RESISTIVE INDEX

TI SCORE	<0.6	0.6-0.69	≥ 0.7
0	18	1	0
1	3	7	0
2	5	20	5
3	0	4	8
4	0	0	0

The degree of tubulo interstitial injury was significantly greater in patients with high normal and high resistive index than in normal group (χ^2=38.89,p=0.001).In contrast little relationship existed between resistive index and Glomerular score (χ^2=2.36,p=0.307.)

RESISTIVE INDEX

GLO.SCORE	<0.6	0.6-0.69	≥ 0.7
0	13	15	5
1	10	10	3
2	3	5	5
3	-	2	-
4	-	-	-

ATROPHIC INDEX AND HISTOLOGIC CHANGES:

As with resistive index the correlation of atrophic index with histologic changes were assessed. In contrast to resistive index , the atrophic index correlated with both tubulo interstitial (χ^2=23.20,p=0.001) and glomerular score (χ^2=15.83,p=0.001)

GLOMERULAR SCORE	<0.65	≥0.65
0	23	4

1	9	20
2	2	10
3	1	2
4	-	-

TI SCORE	**<0.65**	**≥0.65**
0	17	3
1	10	12
2	7	10
3	2	10
4		

COMBINATION OF RESISTIVE AND ATROPHIC INDICES

To determine whether resistive index and atrophic index were independent parameters the correlation between them was examined. As shown below the correlation between them was statistically significant ($r=0.358$, $p< 0.01$). This suggested that both are dependent variables in detecting tubulo interstitial injury. To confirm the above said observation subjects were divided into two groups where both resistive and atrophic indices were normal and one or other high. In this sensitivity and specificity remained low (62%,76% respectively)

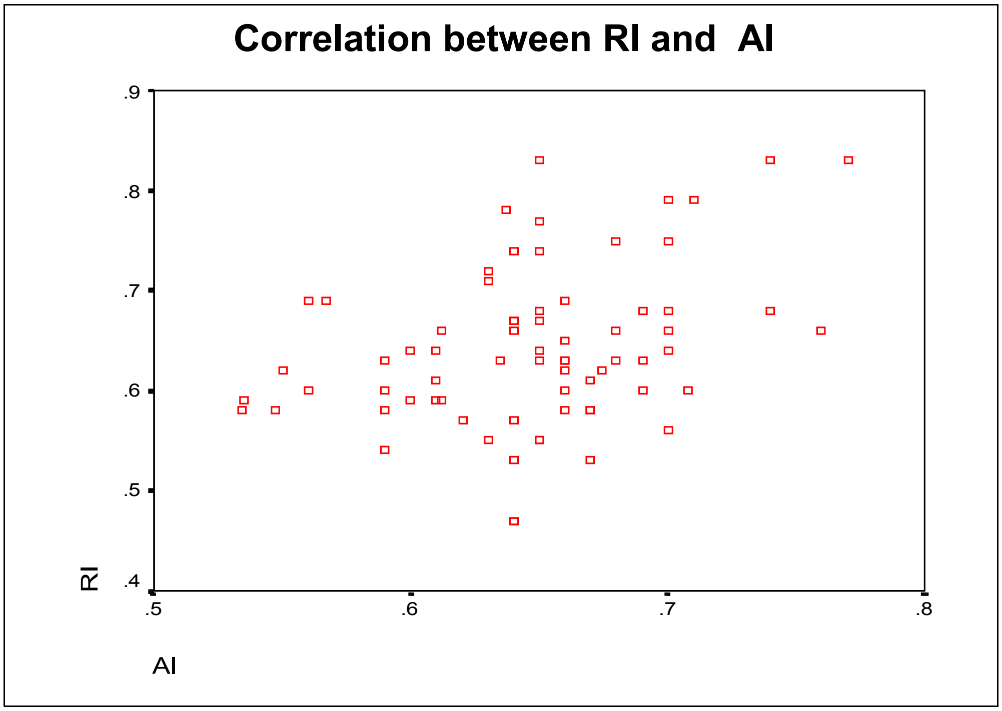

Fig - 3 Correlation of the resistive and atrophic index. Statistically significant correlation was evident between the resistive and atrophic index.

RESISTIVE INDEX AS A MEASURE OF PROGRESSION

The rate of renal function decline in glomerular diseases is highly variable[16]. Predicting future decline in renal function is important for subsequent therapeutic decision.

In general presence of hypertension, renal failure at diagnosis, old age, severe proteinuria, male sex have been shown to predict progression[16]. All progressive renal diseases are associated with interstitial fibrosis hence associated with elevated resistive index . We tested the value of resistive index and atrophic index in predicting progression. In univariate analysis old age, smoking, nephrotic proteinuria, raised resistive index & atrophic index were associated with progression. Cholesterol, hypertension, body mass index, gender were not found to be significant. In multivariate analysis only raised resistive index, atrophic index and nephrotic proteinuria found to predict progression with odds ratio of 23.3, 11.8 and 10.2 respectively

DISCUSSION

This prospective study demonstrated that extent of tubulointerstitial injury can be predicted by measurement of resistive and atrophic indices .One important point is that we focused on tubulointerstitial rather than glomerular lesions .Renal parenchymal resistances measurable by resistive index , represent global resistance offered to blood flow by different parenchymal structures. This is especially true for vasculo-interstitial compartment , since resistive index does not increase if the damage is confined to glomeruli [2] Previous studies reported that presence of interstitial diseases could elevate the resistive index significantly [15]. Our present study supports these results. Combination of these two has not been proven to be useful than either index alone in contrast to similar study[14]This study has also shown good correlation between resistive index and atrophic index which may be the reason for the above finding.

Our study reconfirmed the fact that resistive index correlated well with tubulointerstitial injury than glomerular injury. The tubulointerstitial injury is the best histologic correlate of long term renal survival[18] hence if taken together resistive index should be able to predict long term renal outcome. This is again evident from this study. By multivariate analysis we have demonstrated that elevated resistive index, atrophic index and nephrotic proteinuria portend poor prognosis.

We used resistive index O.60 as a cut off point instead of 0.7.The mean resistive index of our healthy population (109 subjects) was 0.59± 0.03. Our ROC curve found 0.6 as the best discriminatory value. More over as stated earlier a different value may be more appropriate in individual diseases[15]

For example in obstruction to differentiate obstructive system from unobstructed resistive index of 0.7 found to be most appropriate with sensitivity of 92% and specificity of 88%[3].On the other hand in Reno vascular hypertension a value of 0.8 or more strongly predicted lack of improvement after revascularisation.[10]

The present study shows that resistive index of 0.6 should be accepted as a cut off value in glomerular disease in our population. Neither a baseline resistive index data nor in glomerular disease was available in our population .To our knowledge this is the first study to propose such a cut off resistive index in Indian population.

We have also tested the value of atrophic index which can be easily measured at bed side. Renal length has been the most commonly used measurement to identify atrophic changes in renal parenchyma. However in some cases renal length can be normal while parenchyma can be relatively thin. To circumvent this problem this new index was created. By ROC analysis the optimal discriminatory value was 0.65 which was again lower than in comparison with similar study[14]. The significance of atrophic index in glomerular diseases requires further research.

The relationship between age and tubulo interstitial disease also was considered. In the present study no statistically significant difference is evident between the group with tubulo interstitial changes and the group without these changes .ROC analysis showed no optimal value of age for discriminating tubulointerstitial injury (data not shown).Based on these results we concluded that we could ignore the influence of age

Our study had few potential limitations. The Doppler and pathologic analyses were carried out by a single observer. It is well known fact that both are observer dependent, hence significant intra observer variability does exist. This should be borne in mind while interpreting the results of this study.

The median follow up in the study is 8 months which is too short a period to assess progression. Hence more data needed before pronouncing resistive index as a prognostic marker. We used serum creatinine as a marker to measure glomerular filtration rate, the limitations of which is well known.

CONCLUSION

1. We conclude that resistive and atrophic indices can be used to predict the presence of tubulointerstitial lesion in glomerular disease with high sensitivity and specificity.

2. There is a good correlation between resistive and atrophic indices. The combination of the two has not been found to be superior to either index alone.

3. There is a good correlation between resistive index and severity of the tubulo interstitial injury.

4. Resistive index and atrophic index can be useful as prognostic markers to identify patients at risk of progression.

5. Hence whenever possible Doppler might be considered as a supplementary diagnostic and prognostic tool in glomerular diseases

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